PATENT SPECIFICATION

815,538

Date of Application and filing Complete Specification: Aug. 22, 1957.

No. 26486/57.

Application made in Germany on Aug. 25, 1956.

Complete Specification Published: June 24, 1959.

Index at acceptance:—Classes 2(3), C2(A1:A2:A5:B30:R15), I3; and 81(1), E1C(1C:3A4:3B3:4A3:4A4:5B:5C:5D:11:12:13:17).

International Classification:—A61l. C07f.

COMPLETE SPECIFICATION

N-Nitroso-Hydroxylamines and Fungicidal Agents

We, BADISCHE ANILIN- & SODA-FABRIK AKTIENGESELLSCHAFT, a Joint Stock Company organised under the laws of Germany, of Ludwigshafen on Rhine, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to N-nitroso-hydroxylamines and new fungicidal agents.

It is already known that salts of N-aryl-N-nitroso-hydroxylamines have fungicidal action.

We have found that N-nitroso-hydroxylamines and their salts of the general formula $R—\underset{\underset{NO}{|}}{N}—O—X$, in which R represents an aliphatic, araliphatic or cycloaliphatic radical and X hydrogen, one equivalent of a metal or an alkyl-mercury, alkoxyalkyl-mercury, aryl-mercury, halogen-mercury or an ammonium or substituted ammonium radical, are excellent fungicides which are superior to the corresponding aryl-substituted compounds as regards their effect and stability. As compared with the compounds of the aromatic series known from the U.S. Patent Specification No. 2,635,978, the fungicides according to the present invention are also characterised by smaller toxicity. Said Patent Specification No. 2,635,978 describes methods for protecting seeds, plants and fruits from being attacked by microorganisms like bacteria and fungi, which comprises treating them with salts of the N-nitroso-N-phenyl-hydroxylamine or its derivatives, wherein the phenyl radical is substituted by several substituents.

Highly active aliphatic and cycloaliphatic substituents R are for example methyl, isopropyl, benzyl, butyl, cyclohexyl, hydroxymethyl-cyclohexyl, cyano-cyclohexyl-, cycloheptyl and cyclo-octyl radicals. As the substituent X there are suitable, besides hydrogen and ammonium, for example alkyl-ammonium or cycloalkyl-ammonium, one equivalent of the monovalent or polyvalent metals of the groups IA to VIIA and VIII of the Periodic Classification (Mendeleef), as for example sodium, potassium, calcium, barium, cerium, iron and nickel, or of the groups IB to IVB of the Periodic Classification (Mendeleef), as for example silver, copper, zinc, mercury, aluminium, lead, and also alkyl-mercury, alkoxyalkyl-mercury, aryl-mercury and halogen-mercury. These N-nitroso-hydroxylamines may be prepared for instance according to the method as described and claimed in the specification of Application No. 25496/57 (Serial No. 815,537).

The N-alkyl- and N-cycloalkyl-N-nitroso-hydroxylamines are suitable according to this invention for the protection of substrates endangered by injurious fungi, such as cultivated plants, fruit, paper, textiles, glue, tanning liquors, leather, wood, mechanical wood pulp, synthetic substances or emulsions of synthetic substances, lacquers and the like. Depending on their solubility and purpose of use they may be used in known manner in aqueous solution or dispersion, dissolved in oil or as an oily solution emulsified in water, or in the form of preparations, capable of being scattered or dusted, in admixture with inert materials, such as talc, clay or shale meal. Wetting agents, as for example alkyl or aryl sulphonates, and adhesives based on resins, wood ethers, waxes, or the like, may also be incorporated in the preparations.

The fungicidal activity of the compounds is illustrated in the following Examples, but the invention is not limited to these Examples.

EXAMPLE 1

Finely ground mixtures of talc with increasing amounts of active substance of the

[Price 2/-]

compositions specified in the Table are dusted with the addition of spores of the mould fungus *aspergillus niger*, onto nutrient agar, 17 mg of each mixture of active substance, talc and spores being used for each square centimetre. The growth of the fungus was determined after incubation for 5 days at 35° C. In Table 1,

+ + + indicates full fungus growth; dense-closed mycelium cover,
+ + indicates slightly inhibited fungus growth; thin or loose mycelium cover,
+ indicates strongly inhibited fungus growth; only isolated small mycelium islands, and
– indicates total inhibition of the fungus growth.

TABLE 1

Growth of *aspergillus niger*

R=	When using R—N(NO)—O—X in which X=one equivalent of	Percentage content of active substance in the mixture of active substance and talc: 0.075	0.15	0.31	0.63	1.25	2.5	5
isopropyl	cyclohexyl-ammonium	+++	+++	+++	++	—	—	—
isopropyl	copper (II)	+++	+++	—	—	—	—	—
cyclohexyl	hydrogen	+++	++	—	—	—	—	—
cyclohexyl	sodium	+++	+++	—	—	—	—	—
cyclohexyl	potassium	+++	+++	—	—	—	—	—
cyclohexyl	ammonium	+++	+++	—	—	—	—	—
cyclohexyl	calcium	+++	+++	++	—	—	—	—
cyclohexyl	copper (II)	+++	+++	+	—	—	—	—
cyclohexyl	mercury chloride (HgCl)	++	++	+	—	—	—	—
cyclohexyl	zinc	+++	+++	+++	—	—	—	—
cyclohexyl	lead (II)	+++	+++	—	—	—	—	—
cyclohexyl	cyclohexyl-ammonium	+++	+++	—	—	—	—	—
cyclohexyl	cerium (III)	++	++	++	—	—	—	—
cyclohexyl	barium	++	++	++	—	—	—	—
cycloheptyl	ammonium	+++	+++	—	—	—	—	—
cycloheptyl	copper (II)	+++	+++	++	+	—	—	—
cyclo-octyl	ammonium	+++	+++	++	—	—	—	—
cyclo-octyl	copper (II)	+++	+++	+++	+++	—	—	—
cyclo-octyl	zinc	+++	+++	++	—	—	—	—
benzyl	ammonium	+++	+++	—	—	—	—	—
benzyl	copper (II)	+++	+++	++	+	+	—	—
methyl	copper (II)	+++	+	—	—	—	—	—

TABLE 1—*continued*

Growth of *aspergillus niger*

R=	When using R—N(NO)—O—X in which X=one equivalent of	Percentage content of active substance in the mixture of active substance and talc: 0.075	0.15	0.31	0.63	1.25	2.5	5
1-hydroxy-methyl-cyclohexyl	copper (II)	+++	+++	+++	++	—	—	—
For comparison:								
phenyl	ammonium	+++	+++	++	+	—	—	—
phenyl	copper (II)	+++	+++	+++	++	+	—	—
phenyl	zinc	+++	+++	++	+	—	—	—

control without active substance +++

EXAMPLE 2

Leaves of grape vines in pots are sprayed with aqueous dispersions of a finely ground mixture of 80 parts by weight of the copper salt of N-cyclohexyl-N-nitroso-hydroxylamine and N-isopropyl-N-nitrosohydroxylamine and 20 parts by weight of sodium lignin sulphonate. For comparison the corresponding mixture of the copper salt of N-phenyl-N-nitrosohydroxylamine is used. After the sprayed coating has dried, the underside of the leaves is infected by spraying on a spore suspension of grape vine fungus (*plasmopara viticola*). To intensify the infection conditions, the plants are then kept for 12 hours in a chamber saturated with water vapour at 20° C. After remaining for 8 days in the greenhouse at temperatures varying between 20° and 30° C, the plants are again placed in the said moist chamber for 12 hours to intensify the outbreak of spores. Counting the spore positions on the undersides of the leaves gives the following results.

at a concentration of the spraying solution of	% of attacked leaves after treatment with the copper salt of: N-cyclohexyl-	N-isopropyl-	N-phenyl-
	N-nitrosohydroxylamine		
0.125 %	0.0	0.0	4.3
0.063 %	1.0	0.0	24.0
0.031 %	7.3	0.0	25.0
0.016 %	13.4	16.4	46.1

Control 54.7

EXAMPLE 3

30 grams of finely grated orange peel are extracted for 2 hours with 120 grams of water. The filtrate is made up to 1 litre with water and 30 grams of agar added. After sterilisation at 100° C, it is introduced in a flat layer in 3 cc batches into Petri dishes. To the 3 cc of agar contained in each dish there is added 0.2 cc of active substance solution or dispersion of the contents given in the following Table 2.

Infection is carried out by dusting the surface of the agar with spores of green citrus mould (penicillium italicum). After incubation for 8 days at 25° C, the fungus growth given in Table 2 has taken place. In this Table,

+++ indicates a luxuriant mycelium cover
++ indicates a loose mycelium cover
+ indicates only isolated small mycelium islands and
— indicates no mycelium (total inhibition).

TABLE 2

Growth of *penicillium italicum:*

when using R—N(NO)—O—X in which R=	X=one equivalent of	Percentage of the active substance in the solution of the active substance: 0.05	0.1	0.25
cyclohexyl	ammonium	—	—	—
cyclohexyl	sodium	—	—	—
cyclohexyl	calcium	—	—	—
cyclohexyl	copper	—	—	—
cyclo-octyl	ammonium	±	—	—
Comparison:				
phenyl	ammonium	+++	—	—
phenyl	copper	+++	++	++

Control without active substance addition +++

EXAMPLE 4

Oranges are dipped in solutions or dispersions of active substances of the contents given in Table 3. After the coating has dried, they are dusted with spores of green citrus mould and then stored in a moist chamber at 25° C to intensify the infection conditions. The attack of the fruit after 8 days is given in the Table corresponding to the gradations:

+++ =closed mycelium cover,
++ =loose mycelium cover,
+ =isolated mycelium islands,
(+) =slight traces of mycelium and
– =no mycelium (total inhibition).

TABLE 3

Growth of *penicillium italicum:*

when using R—N(NO)—O—X in which R=	X=one equivalent of	Percentage content of active substance in the active substance solution 0.2	1	2
cyclohexyl	ammonium	+++	—	—
cyclohexyl	calcium	+++	—	—
cyclohexyl	copper	+++	—	—
cyclo-octyl	ammonium	++	±	—
Comparison:				
phenyl	ammonium	+++	++	(+)—
phenyl	copper	+++	+	(+)—

Control (Fruit dipped in water without active substance) +++

EXAMPLE 5

25% dilutions of polyvinyl pyrrolidone (K-value 30) have added to them fungicidal additions and are then kept for 8 weeks at 25° C after inoculation with a mixture of mould fungus spores. The fungus growth is as shown in Table 4 corresponding to the gradations:

++ = as without active substance
+ = isolated colonies
(+)− = 1 small colony
− = total inhibition.

TABLE 4

When using	Fungus growth, mg of active substance in batch 1	3.3	6.7	10	33	67	100	250
N-nitroso-N-cyclohexyl-hydroxylamine ammonium salt	+	—	—	—	—	—	—	—
para-hydroxybenzoic acid methyl ester	++	++	++	++	+	(+)—	(+)—	—

Control without active substance ++

EXAMPLE 6

0.01% by weight of N-nitroso-N-cyclohexylhydroxylamine ammonium salt is added to a 20% aqueous solution of a copolymer of equal parts by weight of acrylamide and methacrylamide. After storage for 3 months at room temperature, the sample is still without any fungus attack, whereas an untreated comparative sample becomes mouldy even after a short time.

EXAMPLE 7

A number of samples, each of 80 grams of a liquid vegetable extract mixture with a 23% pure tanning agent content, consisting of 60 parts by weight of chestnut wood extract and 40 parts by weight of fir bark extract, are made up with water to 1 litre (this tanning solution approximately corresponds to one of the average liquors of a normal dyeing process, which is especially susceptible to mould) and 50 mg of one of the following N-nitroso-N-cyclohexylhydroxylamine salts added: ammonium salt, cyclohexyl ammonium salt, zinc salt and calcium salt. All samples remain free from mould during an observation period of 3 weeks. A comparative sample without any addition exhibits strong fungus attack even after 5 days.

EXAMPLE 8

Strips of cotton twill are impregnated in two passages at 60° to 70° C and a squeezing effect of about 90% with intermediate drying, and after drying for 24 hours, soaked for 24 hours in 100 times the bath with change of water five times per hour at 18°C. The strips of material thus treated are then buried in compost earth and exposed to putrefaction for 14 days at 30° C. When removed from the earth, the strips have changed as may be seen from Table 5.

TABLE 5

Impregnation 1st bath g per litre	2nd bath g per litre	Degree of destruction
N-nitroso-N cyclohexyl-hydroxylamine ammonium salt 10	20 copper acetate	slightly discoloured in places
„ 20	20 copper acetate	unchanged
—	20 copper acetate	moderately attacked, brittle
—	— (control)	total destruction

WHAT WE CLAIM IS:—

1. Any N-nitroso-hydroxylamine or salt thereof of the general formula R—N—O—X
|
NO
wherein R represents an aliphatic, araliphatic or cycloaliphatic radical and X hydrogen, one equivalent of a metal or an alkyl-mercury, alkoxyalkyl-mercury, aryl-mercury, halogen-mercury or an ammonium or a substituted ammonium radical.

2. A fungicide comprising a hydroxylamine or a metal or an alkyl-mercury, alkoxyalkyl-mercury, aryl-mercury, halogen-mercury or an ammonium or a substituted ammonium salt thereof as specified in claim 1 and an inert solid material such as talc, clay or shale meal.

3. A fungicide as claimed in claim 2 and also containing a wetting agent.

4. A fungicide comprising a solution or dispersion of a hydroxylamine or a metal or an alkyl-mercury, alkoxyalkyl-mercury, aryl-mercury, halogen-mercury or an ammonium or a substituted ammonium salt thereof as specified in claim 1 and a wetting agent.

J. Y. & G. W. JOHNSON,
47, Lincoln's Inn Fields,
London, W.C.2,
Chartered Patent Agents.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press.—1959.
Published by The Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.